B cell growth was efficiently costimulated with recombinant soluble BAFF lacking the transmembrane domain. This activity is in contrast to several TNF family members which are active only as membrane-bound ligand such as TRAIL, FasL and CD40L. Soluble forms of these ligands have poor biological activity which can be enhanced by their cross-linking, thereby mimicking the membrane-bound ligand (15). In contrast, cross-linking Flag-tagged sBAFF with anti-FLAG antibodies or the use of membrane-bound BAFF expressed on the surface of epithelial cells did not further enhance the mitogenic activity of BAFF, suggesting that it can act systemically as a secreted cytokine, like TNF does. This is in agreement with the observation that a polybasic sequence present in the stalk of BAFF acted as a substrate for a protease. Similar polybasic sequences are also present at corresponding locations in both APRIL and TWEAK and for both of them there is evidence of proteolytic processing (30) (N.H. and J.T, unpublished observation). Although the protease responsible for the cleavage remains to be determined, it is unlikely to be the metalloproteinase responsible for the release of membrane-bound TNF as their sequence preferences differ completely (21). The multibasic motifs in BAFF (R-N-K-R) (SEQ ID NO:23), APRIL (R-K-R-R) (SEQ ID NO:24) and Tweak (R-P-R-R) (SEQ ID NO:25) are reminiscent of the minimal cleavage signal for furin (R-X-K/R-R) (SEQ ID NO:26), the prototype of a proprotein convertase family (31).

IN THE CLAIMS:

Please cancel claims 1-9, 14, 15, and 17-50 and amend claims 10-13 as follows:

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